HSE and National Poisons Information Centre

Update for Healthcare Providers Synthetic Cannabinoid Receptor Agonists

This document was developed in response to new psychoactive substances known as 'synthetic cannabinoids' being identified in products sold as cannabis on the Irish market. As a result, healthcare providers may experience drug-related emergencies relating to this emerging drug trend.

The medical content contained within this document has been adapted from the Novel Psychoactive Treatment UK Network (NEPTUNE) Clinical Guidelines 'Harms of Synthetic Cannabinoid Receptor Agonists (SCRAs) and Their Management (Abdulrahim & Bowden-Jones, 2016).

The emergence of Synthetic Cannabinoid Receptor Agonists (SCRA)

New psychoactive substances (NPS) are a broad range of drugs that are not controlled by the United Nations Drug Control Conventions. NPS include a wide range of substances which include stimulants, SCRAs, opioids, benzodiazepines (and other sedative-hypnotics), hallucinogens and dissociative type drugs. Many of these substances are intended to mimic the effects of internationally controlled drugs and are sold as 'legal' replacements for them (EMCDDA, 2022). SCRAs were previously sold as 'legal' replacements to cannabis in Head Shops in Ireland but were in fact much more potent than cannabis and increased the physical and mental health risks. By 31 December 2021, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) was monitoring 224 SCRAs that have appeared on the EU drug market since 2008, including 15 that were notified in 2021. This makes them the largest group of substances being monitored in Europe.

During the COVID-19 period, SCRAs began to emerge throughout Europe in products sold as low THC herb, cannabis vape and cannabis edibles. During 2021, sweets containing SCRAs were seized in at least five countries: Belgium, Estonia, Ireland, Slovakia and Sweden (EMCDDA, 2022). While cannabis edibles pose additional risks compared with the inhalation of cannabis, of extra concern is the emergence of SCRAs being sold unknowingly to different user groups across the Irish market and an alert was issued at the start of 2023 regarding hospitalisatoons associated with this trend.

There is currently a high risk of SCRAs being sold as cannabis in Ireland as herb, vape and edible products.

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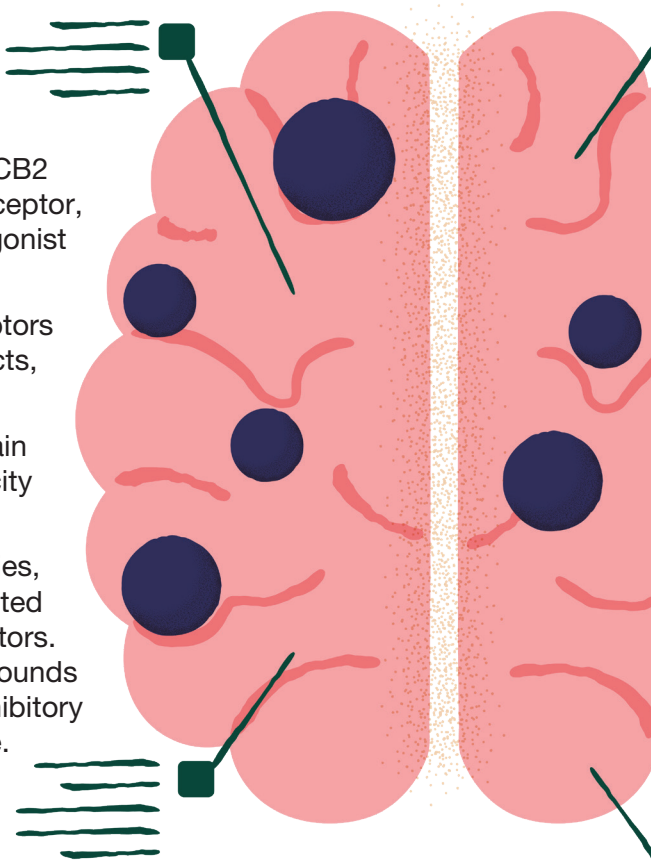
Pharmacology and effects of SCRAs

Synthetic cannabinoid receptor agonists (SCRAs) are a large group of drugs, which have a strong effect on the endocannabinoid system. With some functional similarity to cannabis, the chief psychoactive constituent of which is delta9-tetrahydrocannabinol (THC), as well as to other phytocannabinoids. However, many of the SCRAs are not structurally related to cannabinoids or THC.



- Both SCRAs and cannabis (THC) bind to the CB1 and CB2 receptors in the brain. The greater the affinity to the CB1 receptor, the higher is the psycho-pharmacological activity of the agonist compound.
- SCRAs usually have a much higher affinity for those receptors than cannabis. As a result, SCRAs can produce stronger effects, especially those that act as full agonists on the CB1 receptor.
- SCRAs may have other biological actions, which may explain some of the differences in severity and features of toxicity between SCRAs and cannabis.
- Some SCRA compounds incorporate indole-derived moieties, which are structurally similar to serotonin and may be associated with particularly high levels of activation of serotonin receptors. It has been suggested that at high doses some SCRA compounds may also possess monoamine oxidase and 5-HT reuptake inhibitory properties, which may increase the risk of serotonin syndrome.
- In contrast to cannabis, SCRAs do not contain cannabidiol (CBD), a chemical which may moderate the effects of THC and may possess anxiolytic, antipsychotic and anti-craving properties.
- It has been reported that, in comparison with cannabis, SCRAs are characterised by quicker onset of effects, significantly shorter duration of action, worse hangover effects and more intense visual hallucinations, paranoid feelings and behavioural disturbances.
- Most SCRAs are more potent than cannabis, and some have long half-lives. There are differences between the various SCRAs, with some having significantly greater potency than others. Products containing SCRAs can range from those with potency similar to cannabis to those that are up to 100–800 times more potent than cannabis typically is.

(Abdulrahim & Bowden-Jones, 2016)

Duration of action

- There are wide differences between the various SCRAs, including in metabolism, potency, toxicity and duration of effects. CRAs can range from 1–2 hours for some compounds to up to 6–8 hours for others.

Acute Toxicity

Acute SCRA toxicity appears to have a similar clinical presentation to the toxicity of cannabis and THC, although differences have been reported, with convulsions and hypokalaemia particularly noted.

People who ingest SCRAs may develop an adverse effect that requires an intervention. Even when the person presents with symptoms of SCRA intoxication, these will usually be self-limiting and resolve spontaneously.

However, SCRA products can have unpredictable effects. There is also evidence that some more recent formulations may be more potent than earlier ones and be associated with greater harms.

Symptoms of acute toxicity

Neurological, cognitive and psychiatric effects

- Anxiety, irritability and psychosis-like effects
- Depression and suicidal thoughts, excitability, agitation, combativeness, aggressiveness, thought disorganisation, panic attacks, paranoid thinking, delusions and auditory and visual hallucinations, changes in perception
- Reduced levels of consciousness and coma
- Numbness, tingling, light-headedness, dizziness, pallor, tinnitus, diaphoresis, tremor, somnolence, syncope, unresponsiveness, nystagmus and convulsions
- Short-term memory and cognitive deficits, confusion
- There are reports of SCRA-associated acute transient psychosis, as well as reports that some individuals may experience psychosis that persists for weeks after the acute intoxication, or even longer.
- Psychosis has been reported in otherwise healthy people; however, there is particular concern about the risk of SCRAs precipitating psychosis in vulnerable individuals, including those with a current or previous history of psychosis.
- In comparison with psychotic episodes associated with the use of cannabis, psychotic episodes associated with SCRAs occur more frequently, are more severe and are linked to greater agitation.

Cardiovascular effects

- Tachycardia, hypertension, hypotension, hypokalaemia, chest pain and palpitations, myocardial ischaemia, myocardial infarction, ischaemic strokes
- Neuromuscular and musculoskeletal effects
- Hypertonia, myoclonus, myalgia, rhabdomyolysis

Renal effects

- Acute kidney injury
- The use of SCRAs should also be considered in atypical presentations, such as acute unexplained kidney injury or myocardial infarction in an otherwise healthy young person.

Other effects

- Hyperglycaemia, hypoglycaemia, acidosis, respiratory acidosis, cold extremities, dry mouth, dyspnoea, mydriasis, vomiting, loss of sight and speech

Serotonin syndrome

- SCRAs have been linked to serotonin syndrome. Serotonin syndrome is a potentially life-threatening condition precipitated by the use of serotonergic drugs. It may be a consequence of therapeutic medication use, interactions between medications or recreational drugs, or intentional overdose. Symptoms can range from mild to fatal and classically include altered mental status, autonomic dysfunction, and neuromuscular excitation.

(Simon and Keenaghan, 2023; Schifano et al., 2021).

Managing acute intoxication and toxicity

For up-to-date information on the management of the harms of SCRAs consult TOXBASE® (www.toxbase.org).

The management of SCRA toxicity is symptomatic and supportive, as no antidotes exist.

- Hydration and monitoring may be enough for patients with mild to moderate intoxication
- Supportive treatment is dependent on a patient's specific presentation (e.g. agitation, delirium, hypertension, convulsions).
- In a minority of cases, SCRA consumption can be associated with severe cardiovascular, cerebrovascular, neurological, psychiatric and renal effects.
- Interventions will focus on the prevention of rhabdomyolysis and the monitoring of cardiac or cerebral ischaemia.

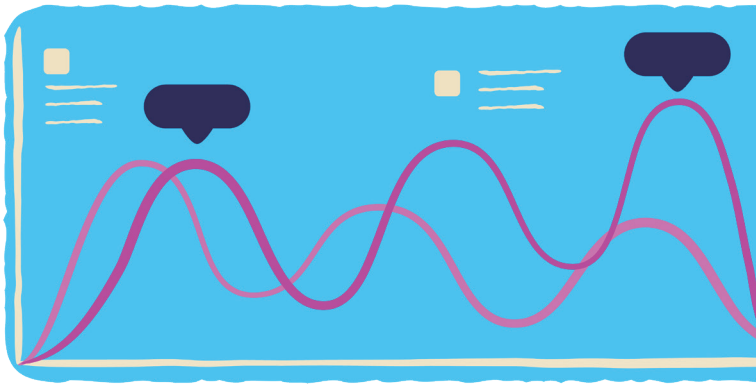
(Abdulrahim & Bowden-Jones, 2016)

The National Poisons Information Centre of Ireland

The National Poisons Information Centre provides information to doctors and healthcare professionals, to assist them in the management of acute poisoning.

Please contact the National Poisons Information Centre on 01 8379964/6 in cases of patients with severe/unusual features or if multiple patients present together. This phone line will be in operation 24 hours and 7 days a week.

Substance analysis



- Identification and assessment of acute harms in acute care settings SCRAs cannot be detected by the routine screening tests for THC, the active ingredient in cannabis.
- Clinicians working in emergency care should be vigilant for SCRA-induced toxicity despite negative drug-screening results.
- Base your diagnosis of acute SCRA intoxication on clinical assessment and recognition of symptoms of toxicity. Do not depend on urinalysis unless conducted within a laboratory.
- Many new SCRA compounds may not appear in existing tests for SCRAs.

- Determine ingestion mode of SCRAs which could be part of a polydrug pattern. They are currently appearing predominantly in edible and vape products sold as cannabis which could interact negatively with other substances.
- SCRAs could emergence across the drug market without consumer's knowledge. There is currently a high risk of SCRAs being sold as cannabis (herb, vape and edibles).
- If SCRA exposure or the exposure to other potent new psychoactive substances is suspected, urine or blood samples should be collected as soon as possible and stored for further review to contribute to the review of the Irish early warning system. Alternatively, patients could be requested to provide to remaining samples of the substances to clinicians for analysis.

References

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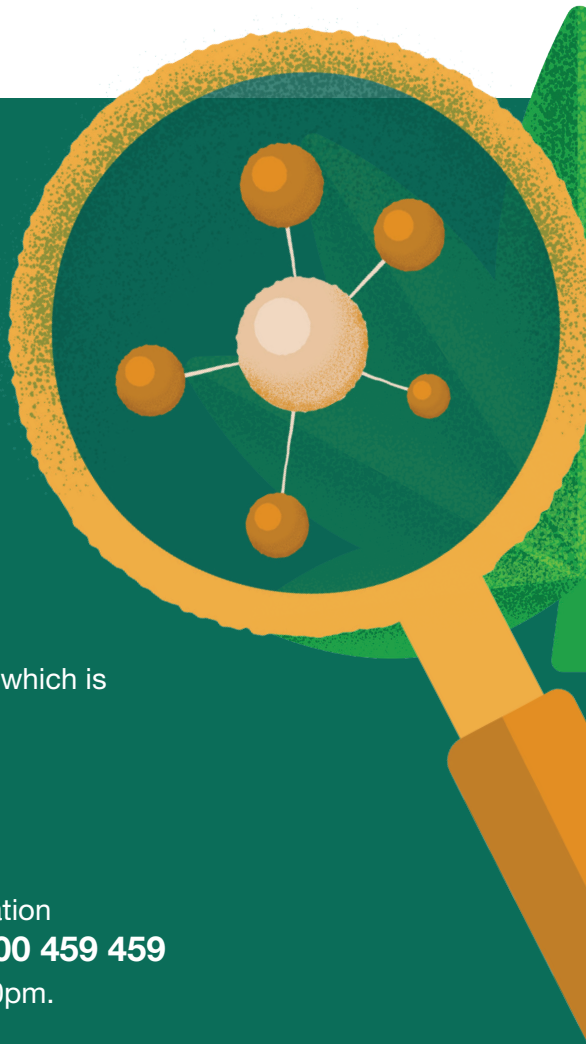
Additional supporting information



Where concerning or dependent use has been identified, signpost or refer to specialist drug treatment and recovery services, a list of national services can be found on online at **www.drugs.ie/services**

Information about different types of drugs and how to minimise harm can be found on the **Drugs.ie** website.

Information about cannabis edibles can be found in the HSE factsheet which is available online to download from the webpage **www.drugs.ie/resources/factsheets/**

Information about synthetic cannabinoids is available online **here**

The **HSE Drug and Alcohol Helpline** is available to offer information and support to people who use and their loves ones on Freephone **1800 459 459** or through email at **helpline@hse.ie** Monday – Friday 9:30am – 5:30pm.

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